



Vitamin D Deficiency and its Association with Respiratory Tract Infections in Pediatrics

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Abstract: Respiratory tract infections (RTI) are a major cause of mortality and morbidity in children. Several studies have aim supplementation as a possible preventive measure against respiratory tract infections in children. Vitamin-D (sunshine vitamin) is a type of prohormone with various functions like extracellular calcium ion maintenance, immunomodulation in the body. The three major sources of Vitamin-D are Sun exposure, Diet and Supplements. The main objective of our study was to correlate the vitamin D deficiency in children with RTI's. A prospective observational study was conducted for 6 months inpatient of the Pediatric department in tertiary care hospital. Demographic details, cause of admission, past medical and medication history, feeding history, sun exposure was taken by interviewing the guardian. Data of a total of 25 pediatric patients with various respiratory tract infection cases were collected, documented and their vitamin D levels were analyzed in our study. The vitamin D level of samples was analyzed by Electro chemiluminescence immunoassay. Statistical methods were applied and significant differences were observed among the vitamin D sufficient and deficient patients with RTI's. It was observed that out of 25 cases, 16 cases had recurrent respiratory tract infections and 9 had non-recurrent respiratory tract infections which statistically shows P value < 0.05. This study significantly correlates vitamin D deficiency with respiratory tract infections in children. This study also suggests vitamin D as a supplement therapy as it plays an important role in the innate and the adaptive immunity.

Key words: Respiratory Tract Infections, Vitamin D, Prospective, Electrochemiluminescence Assay, Immunomodulation.

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I. INTRODUCTION

Respiratory tract infections are a major cause of mortality and morbidity in children. Several studies states that lower levels of vitamin D is associated with an increased risk of RTI's. Vitamin-D (sunshine vitamin) is a type of prohormone with various functions in the body. Prohormone refers to a group of Fat soluble secosteroids.

I.1 The two major forms of vitamin-D are

- 1) Vitamin D₂ (ergocalciferol)
- 2) Vitamin D₃ (cholecalciferol)¹

RTIs are also a major cause of hospitalization in children younger than 5 years, especially in infants whose rate of hospitalization was about 1.3 times higher than the overall rate in children aged 0–59 months, causing a substantial burden on health care and impacting early childhood development.²³ According to WHO in 2019 an estimated 5.2 million children under 5 years mostly died from preventable and treatable causes, one of the major cause of death in children is due to respiratory tract infections (Pneumonia)⁸. According to the Public health foundation of India (2017) the major cause of child mortality is lower respiratory tract infections (17.9%)⁹. Epidemiological studies state that low levels of vitamin D is associated with pulmonary function impairment¹⁰. In recent era, micro-nutrients are playing a major role as potential

adjunctive immunotherapy to the polyvalent actions of vitamin D for human deficit has been looked into and has been associated with a number of different diseases¹¹. Most of the studies had concluded that decreased serum concentration of vitamin D is associated with increased rate of respiratory tract infections and decreased levels of vitamin D is seen in children with respiratory tract infections¹². According to the study done by Bergman et al it includes 11 randomized placebo controlled trials. The summarized result shows that vitamin D supplementation significantly decreases the risk of respiratory tract infection¹³. The study conducted by (maruotti) concludes that there is a relation between vitamin D and immune system.¹⁴ However, evidence regarding the effects of vitamin D supplementation on susceptibility of infants and children up to 12 years to RTI is limited. In this prospective observational study, we examined the vitamin D levels of 25 children up to 12 years. The main aim of our study was to estimate the levels of vitamin D in patients with respiratory tract infections and our objective of the study was to find out the susceptibility, severity of reoccurrence of RTI's associated with vitamin D status. The metabolism of vitamin D and its effect on the innate and the adaptive immune system are explained in detail below (Figure 1).

I.2 Sources of Vitamin D

The three major sources of Vitamin-D are Sun exposure, Diet and Supplements.

Table 1: sources of vitamin D:		
S.no	Sources	Examples
1.	Sun exposure	Vitamin D is produced in the skin when exposed to UVA and UV B radiations.
2.	Diet	Oil rich fish such as salmon, Milk, yogurt, cheese, orange juice and cereals.
3.	Supplements	400- 1000 IU/day for children aged less than 1 year. 600-1000 IU/day for children aged ≥ 1 year. 1500-2000 IU/day for adults aged ≥ 19 years.

- Major sources of Vitamin-D are sunlight. Skin produces Vitamin-D when exposed to UV B radiation in summer months for about 10-15 minutes of sun exposure. People with lighter pigmentation will generate 1000-2000 IU of vitamin D within 24 hrs when exposed to the sun for the stipulated time ²
- Lower vitamin D levels are seen in winter due to which there is an increase in respiratory tract infections.

METABOLISM AND PHYSIOLOGICAL ACTIONS OF VITAMIN D:³

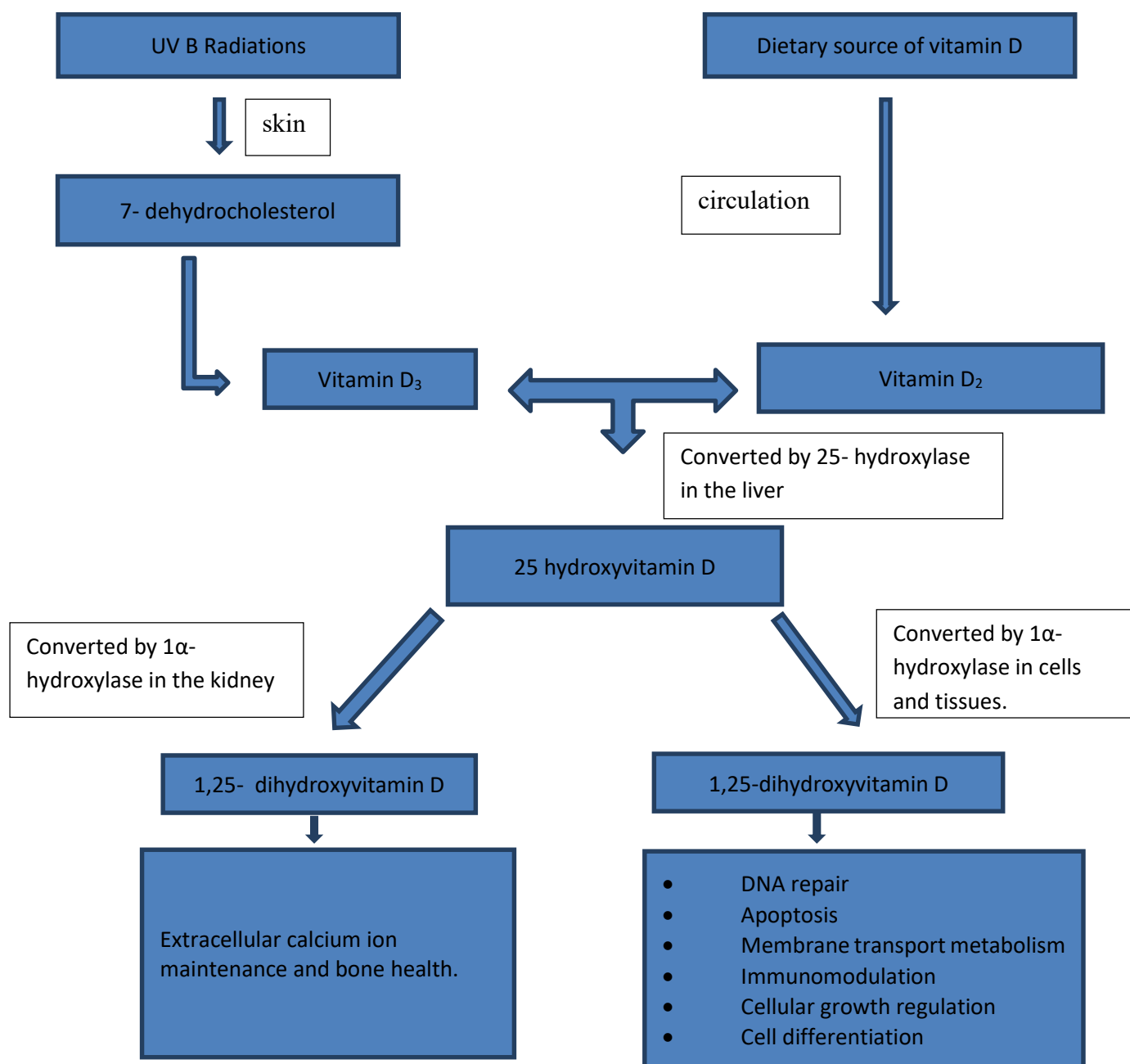


Fig 1: Metabolism of vitamin D

1.3 Role of Vitamin D in Innate and Adaptive Immunity

The active form of vitamin D i.e., 1,25(OH)₂ D plays an important role in the immunomodulatory functions which are mediated through the VDR which is expressed in many cells of the immune system such as T and B lymphocytes, neutrophils, monocytes, macrophages and dendritic cells. Several studies showed that Vitamin D supplementation was protective against various respiratory tract infections. The mechanism by which Vitamin D prevents RTI's is due to increased expression of cathelicidin, regulation of cytokine release and suppression of adaptive response by boosting the innate immune system.⁴ The two important cells in the innate immune system which are involved in the recognition, inactivation, and killing of microorganisms are monocytes / macrophages and dendritic cells. These cells are also involved

in the activation and development of an adaptive immune response as they present the antigens from the pathogen to the resting B and T lymphocytes, which upon activation expresses abundant VDR. Thus, under the influence of 1, 25 (OH)₂ D ,activated B lymphocytes reduce proliferation, immunoglobulin production, memory and plasma cell differentiation. It also promotes the inhibition of T cell differentiation and proliferation, Th 1 cell immune activity and 2 driven B cell immunoglobulin production. These effects results in decreased production of inflammatory cytokines and increased production of anti inflammatory cytokines such as IL 10.⁵ Therefore, 1,25 (OH)₂ D vitamin D stimulates the innate immune response in antigen presenting cells and at the same time it inhibits any overzealous response in the adaptive immune system to the offending antigens.

1.4 Etiology of vitamin D deficiency in children:6

Vitamin D deficiency is common in children because of various factors such as:

- Decreased nutritional intake
- Decreased cutaneous synthesis because of various cultural/ religious practices,

- Climatic changes
- Increased rate of exclusive breastfeeding
- Lower maternal vitamin D levels
- Practice of not taking the child out. This study is designed to estimate levels of vitamin D in patients with respiratory tract infections among and also to correlate the effect of vitamin D deficiency in children with respiratory tract infections.

Currently accepted standards for defining the vitamin D status in children and adolescents are as follows

Table 2: Standard vitamin D value ⁷		
S.no	vitamin D levels	Normal values
1	Vitamin D sufficiency	25 (OH) D $\geq$ 20ng/ml / $\geq$ 50 nmol/l
2	Vitamin D insufficiency	25(OH) D between 15 – 20ng/ml or 37.5 -50 nmol/l
3	Vitamin D deficiency	25 (OH) D between 5- 15 ng/ml or 12.5 -37.5 nmol/l
4	Severe deficiency	25(OH) D $\leq$ 5 ng/ml
5	Risk of toxicity	$\geq$ 150 ng/ml

2. METHODOLOGY

A prospective observational cohort study was performed in the inpatient pediatric department in Gandhi hospital for a period of six months. The study period includes September 2019-February 2020. During this study period overall 25 samples are collected based on inclusion and exclusion criteria. The inclusion criteria include collecting the blood samples from the children who aged between 1-12 years with respiratory tract infections. The exclusion criteria include the children who are already on vitamin D supplementations, and those who have congenital skeletal disorders, congenital heart diseases, congenital lung disorders, renal diseases. Also, the children who are on medications affecting vitamin D metabolism like phenytoin, phenobarbitone and sodium valproate are excluded from the study.

2.1 Study Procedure

The study was carried out by collecting the Respiratory tract infection cases and estimate the vitamin D levels. Study protocol has been submitted to the Institutional ethical committee (IEC), CMR College of Pharmacy, Hyderabad before commencement of the study and Ethical clearance from

the committee was taken with the approval No: CMRCP/IEC/2019-20/05. All procedures performed in the study were conducted in accordance with the ethical standards given in 1964 Declaration of Helsinki, as revised in 2013. A prospective observational cohort study was conducted, which includes regular ward round participation in the department of pediatrics. Based on the inclusion criteria the cases with respiratory tract infections were identified. The identified cases are documented in the data documentation form. The samples were collected from the selected patients and vitamin D levels were observed. The results were supported by statistical analysis of the data.

3. STATISTICAL ANALYSIS

Data of a total of 25 pediatric patients with various respiratory tract infection cases were collected, documented and their vitamin D levels were analyzed in our study. The vitamin D level of samples was analyzed by Electrochemiluminescence immunoassay. A Chi square test was performed in the Microsoft excel to analyze the various parameters. The following tables depict the results of our study obtained from the Chi square test.

4. RESULTS

The following table (Table 3) demonstrates different types of cases as per diagnosis:

Table 3: Distribution of cases as per diagnosis:			
S.no	Type of cases	Number of cases	Percentage (%)
1	Pneumonia	16	64
2	Pulmonary TB	4	16
3	Hyper reactive airway disease	3	12
4	Bronchiolitis	1	4
5	WALRTI	1	4
6	Total	25	100

Data obtained from the above table indicates that most of the cases collected were pneumonia (64%), Pulmonary TB (16%), Hyper reactive airway disease (12%), Bronchiolitis and WALRTI 4% each.

Table 4: The Frequency of deficiency and normal cases			
Vitamin D levels	deficiency	normal	Total
No of cases	21	4	25

Based on the data collected, the cases with vitamin D deficiency levels were 21 and with normal vitamin D levels were 4.

Table 5: Age wise distribution of cases:					
Vitamin D levels	age(1-4)	age(5-8)	age(9-12)	Total	P Value
Deficiency	11	5	5	21	0.532236
Normal	3	0	1	4	
Total	14	5	6	25	

$$X^2=4.3302 \quad P \text{ value} = 0.532236$$

The relation between these variables was not significant as $X^2=4.3302$ which is greater than the P value.

In the above table (Table 5), a total of 25 cases have been distributed according to their age groups. The highest number of cases (14) has been observed in the age group 1-4 years, 5 cases in the age group 5-8 years and 6 cases in the age group

9-12 years. A Chi square test was performed to examine the relation between age group and occurrence of vitamin D deficiency in children with respiratory tract infections.

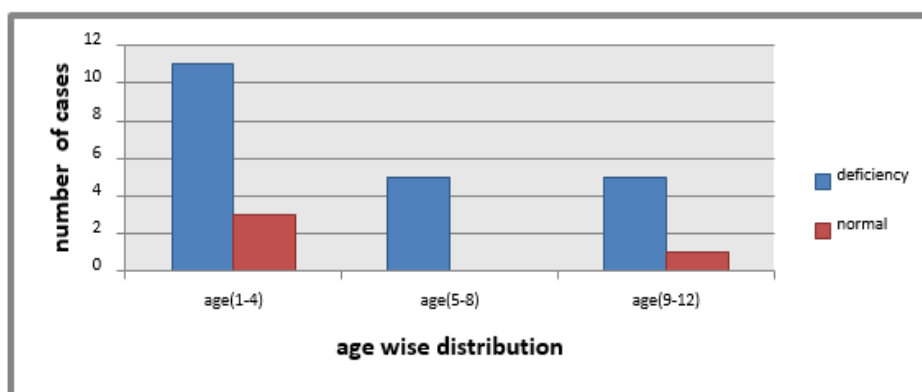


Fig 2: Age wise Distribution of cases

Table 6: Gender wise distribution of cases:				
Vitamin D levels	male	female	total	P values
Deficiency	13	8	21	0.656
Normal	2	2	4	
total	15	10	25	

$$X^2 = 0.3289 \quad P \text{ value} = 0.656$$

Based on the data obtained, out of the 25 cases collected, 15 cases were of female and 10 cases were of male. From the data obtained, it cannot be stated that vitamin D deficiency is found only in a particular gender as $P > 0.05$. Therefore, the relation between these variables is found to be insignificant.

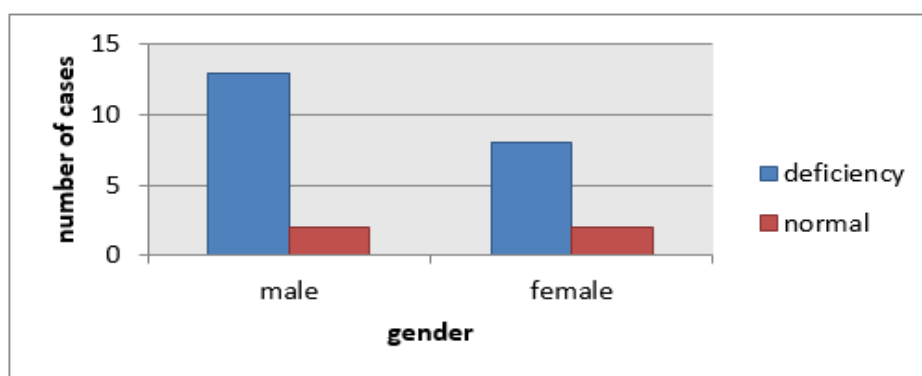


Fig 3: Gender wise Distribution of cases

Table 7: Vitamin D status in recurrent and non recurrent RTI's:				
Vitamin D Level	RRTI	NON RRTI	Total	P Value
Deficiency	15	6	21	0.076
Normal	1	3	4	
Total	16	9	25	

$$X^2=3.2224 \quad P \text{ value} = 0.07$$

The above table (Table 7) shows the distribution of the recurrent and non-recurrent respiratory tract infection cases. Based on the data obtained, it was observed that out of 25 cases, 16 cases had recurrent respiratory tract infections and 9 had non recurrent respiratory tract infections. Since the P

value <0.05 , the relation between the variables was found to be significant. Therefore, we conclude that the vitamin D deficiency is more common in the patients with recurrent respiratory tract infections when compared to non-recurrent respiratory tract infection cases.

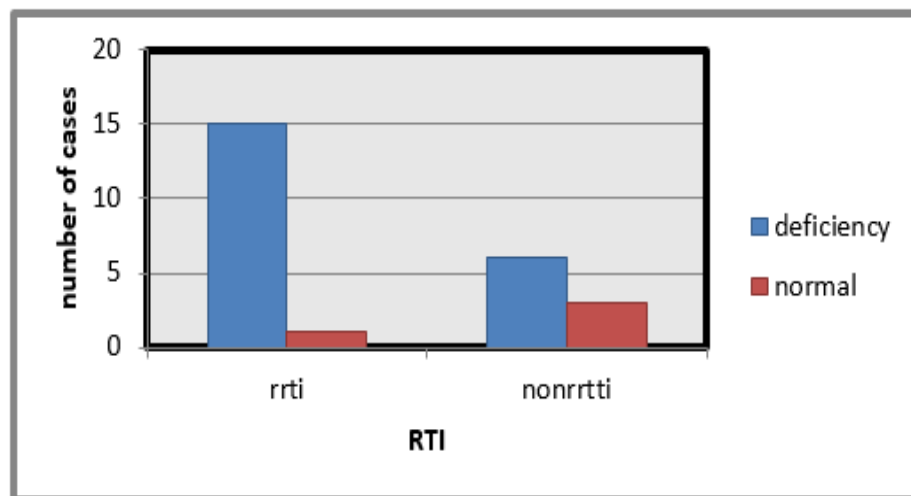


Fig 4: Vitamin D status in recurrent and non recurrent RTI

8:Sun exposure adequacy and vitamin D status of subjects.					
Vitamin D	Adequate exposure	Inadequate exposure	Total	P Value	
deficiency	6	15	21	0.007	
normal	4	0	4		
Total	10	15	25		

$$\chi^2=3.231 \quad P \text{ value } =0.007$$

Based on the data obtained from the above table, 10 out of 25 patients had adequate sun exposure and 15 had inadequate sun exposure. As the P value < 0.05 , the relation between the two variables is found to be significant. Therefore, it can be stated that the children with inadequate sun exposure had more chances of having vitamin D deficiency.

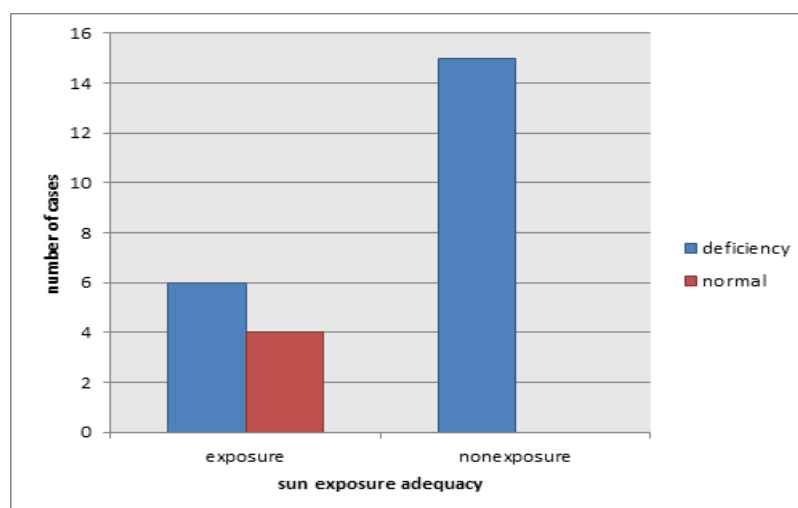


Fig 5: Sun exposure adequacy and vitamin D status of subjects

Table9: Breast feeding status of cases.						
Vitamin D	Exclusively up to 6 Months	Exclusively up to 4 Months	Partial breastfed	Never breastfed	Total	P Value
Deficiency	9	6	5	1	21	0.221
Normal	4	0	0	0	4	
Total	13	6	5	1	25	

$$\chi^2=4.3956 \quad P \text{ value } =0.221$$

The table above shows the breast feeding status of cases. The children who were given exclusive breastfeeding for 6 months were 13, exclusive breastfeeding upto 4 months were 6, partially breastfed were 5 and never breastfed were 1. Since

the P value >0.05 , the relation between the two variables is insignificant. It cannot be ascertained that vitamin Deficiency occurs if the child is breastfed for a particular period of time.

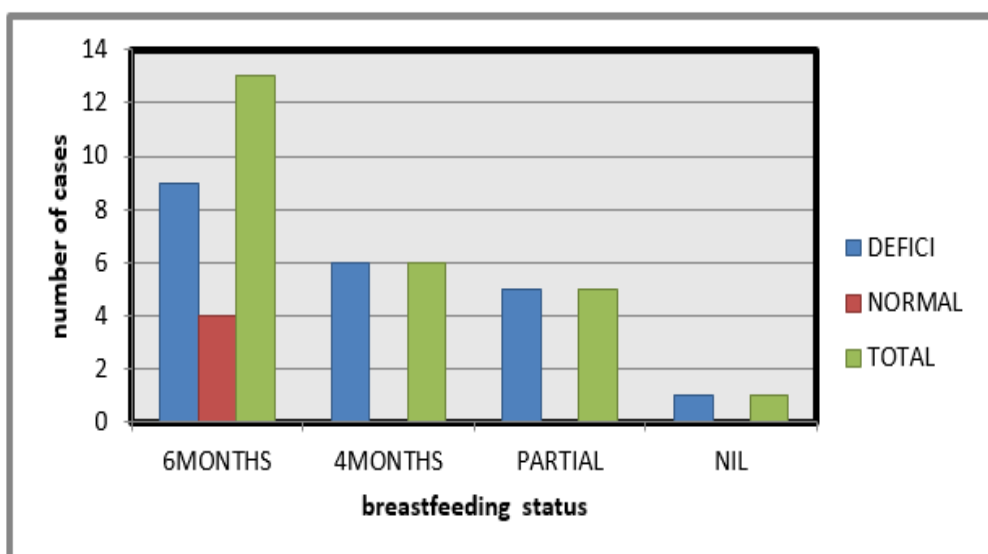


Fig 6: Breastfeeding status of cases

5. DISCUSSION

This study was carried out by analyzing the vitamin D samples of a total of 25 pediatric patients who were admitted with various respiratory tract infections according to our inclusion criteria. Out of the 25 cases collected, 16 cases were diagnosed with pneumonia, 4 cases with tuberculosis, 3 cases with HRAD, 1 case with bronchiolitis and 1 case with WALRTI (table 3). Therefore, based on our data the majority of the cases with vitamin D deficiency were of lower respiratory tract infections. This result is in support with the study conducted by Dr. Chandrasekhar (2019)¹⁵ who stated that there is a significant correlation between vitamin D deficiency and lower respiratory tract infections. Gender wise distribution of the data shows a higher female: male ratio as 15 samples were of female patients and 10 were of male (Table 6). But it cannot be concluded that vitamin D deficiency is prevalent only in a particular gender. Based on the data collected, most of the cases collected were of the age group 1-4 years but based on our statistical data, there was no significant relation of age with vitamin D deficiency (Table 5). These may be regarded as chance findings resulting from the lack of matching cases in terms of age and gender as stated by Wayse V (2004)¹⁶ in his study. This study highlights that vitamin D deficiency was more significant in children with recurrent respiratory tract infections and repeated admissions into the hospital with various respiratory tract infections when compared to children with non-recurrent respiratory tract infections (Table 7, Figure 4). This finding was according to the study conducted by Dr. Alladi YR (2017)¹⁷ who stated that vitamin D deficiency was more prevalent in patients with recurrent respiratory tract infections. It could be concluded that vitamin D plays a protective role against the frequent respiratory tract infections in children as it plays an important role in the innate and adaptive immunity Bergman P (2013), Laaksi I (2010)²⁴. Our study reveals that the vitamin D deficiency is more commonly observed in the samples of children who had lesser exposure to the sunlight when compared to the children with good exposure to the sun. The

information regarding the exposure of sunlight was obtained by enquiring the child's parents whether they had a practice of exposing the infant to sunlight and also about how the child was dressed when exposed to the sun (Table 8). This was explained by Sakamoto RR (2019)¹⁸ in his study which states that sunlight plays a very important role in mitigating the effects of vitamin D deficiency. We observed that the majority of the children who were diagnosed with respiratory tract infections and who had vitamin D deficiency were admitted in the intensive care unit when compared to IPD. Thus, it was observed that children with vitamin D deficiency had more severe conditions. This was also observed in the study conducted by Kulkarni SP in 2017¹⁹. This study included the breast feeding status of the children. It was observed that there was not much difference in the vitamin D levels of children who were exclusively breastfed till 4 months of age and 6 months of age (Table 9, Figure 6). Therefore, no significant correlation was found between breastfeeding and vitamin D levels as it depends mainly on the maternal vitamin D status²⁰. This observation was also supported by the study conducted by Chowdhury R (2017)²¹. Therefore, from our findings we recommend explaining the importance of vitamin D rich food or supplements to the exclusively breastfed mothers and also children to optimize the overall pediatric health as explained by Taylor SN (2020)²² and Camargo CA²⁵

6. CONCLUSION

Our study correlates the effect of vitamin D deficiency in children with respiratory tract infections. It was also observed that vitamin D deficiency is more common in the children with recurrent lower respiratory tract infections. As vitamin D plays an important role in the innate and adaptive immunity, vitamin D can be recommended as a supplement therapy and may also help to prevent the frequent LRTI's and thereby frequent hospital readmissions. Education regarding the importance and timing of sun exposure must be done (half an hour per day for 5-6 days/ week between 10 am to 3 pm) as it is a major source of vitamin D.

7. AUTHOR CONTRIBUTION STATEMENT

Dr. G. Ramya conceptualized the work and gave necessary inputs in designing the study. Alekhya Muliki and Sanjana Reddy gathered the data with regard to this work. Jumana Hakeem and Avanish Illuri analyzed these data and designed the manuscript. Dr. Pradeep gave the necessary assistance in collecting the vitamin D samples from the children diagnosed

9. REFERENCES

- Esposito S, Lelli M. Vitamin D and respiratory tract infections in childhood. *BMC infectious diseases*; (2015), 15: 487. Available from : <https://www.ncbi.nlm.nih.gov/pubmed/26521023>
- Mahomed G .Vitamin D in respiratory diseases' *Afr Respir*, (2017); 23:14-18. Available From: <http://www.ajtccm.org.za/index.php/SARJ/article/download/122/116>
- Ahmed A.M.S, Association of Vitamin D status with acute respiratory infection and diarrhea in children less than two years of age in an urban slum of Bangladesh , PhD thesis, school of Public Health. The University of Queensland.Availablefrom: https://espace.library.uq.edu.au/data/UQ_400590/s4277819_final_thesis.pdf?Expires=1590070102&Key-Pair-Id=APKAJKNB4MJB4JNC6NLQ&Signature=PgVD7MhrXjB5R-FnxNWIZbALjTd5aTUElQe6NE9PSTdbSWACVeGg0AuQwh6OlvtDRklCBhwNN~BGIM8EoILkyZdRpBzN~EdDwLdc2akqtGnUQiwXW2nQiCz8yFoWcwQSLzD85cLbOpDql0SveapCzgnNN~YX44gIFqB~3Dmxf2joYYQBIO44RbhviPcW~jJwlr3hXhKXfhDILKl8rC9tvRydtfNGWzAdXo8OApuNibWnfzrkotyijXrDhgSughnpiVdhqtzVlthvBz8J~e4nTpcgMdYucmeUVQS05D2iMVKdCtfgvEPxNuGzOMB9AGku-bVp63pTEv5aSB2ZZZw_
- Martens PJ, Gysemans C, Verstuyf A, Mathieu AC. Vitamin D's Effect on Immune Function. *Nutrients*. 2020 Apr 28;12(5):1248; PMID: PMC7281985.DOI:<https://doi.org/10.3390/nu12051248>
- Aranow C. Vitamin D and the immune system. *J Investig Med*. 2012 August; 59(6): 881-886.Available from:<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3166406/>
- Balasubramanian S, Dhanalakshmi K, Amperayan S. vitamin D deficiency in childhood. *Indian pediatr* (2013); 50:660-675. Available from: <https://www.indianpediatrics.net/july2013/july-669-675.htm>
- Lee JY, So TY, Thackray J. A review on vitamin D deficiency treatment in pediatric patients. *J Pediatr Pharmacol Ther*. 2013;18(4):277-291.Available from: doi:10.5863/1551-6776-18.4.277
- World Health Organization. Children Improving Survival and Well-being [internet]. 2020 Available from: <https://www.who.int/news-room/fact-sheets/detail/children-reducing-mortality>
- <https://phfi.org/district-level-trends-of-child-mortality-and-child-growth-failure-in-india/>
- Herr C, Greulich T, Koczulla RA, Meyer S, Zakharkina T, Branscheidt M, Eschmann R, Bals R. The role of vitamin D in pulmonary disease: COPD, asthma, infection, and cancer. *Respir Res*. 2011 Mar 18;12(1):31.

with Respiratory Tract infections. All the authors discussed the methodology and results and contributed to the final manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

- DOI: <https://doi.org/10.1186/1465-9921-12-31>
- Dini C, Bianchi A. The potential role of vitamin D for prevention and treatment of tuberculosis and infectious diseases. *Ann Ist Super Sanita*. 2012;48(3):319-27. DOI:https://doi.org/10.4415/ann_12_03_13
- Pratima K, Ambedakar S N, Mohapatra J.Vitamin D deficiency among hospitalized infants with acute lower respiratory tract infections. *Int J Contemp Peadiatr*. (2020):1589-1592.DOI: <http://dx.doi.org/10.18203/2349-3291.ijcp20202622>
- Bergman P, Lindh A U, Bergman B ,Lindh J D. Vitamin D and Respiratory tract infection:A Systematic Review and Meta analysis of Randomized controlled trials . *PLOS ONE* June (2013) 8(6):e65835.DOI :<https://doi.org/10.1371/journal.pone.0065835>
- Maruotti N Cantore F P. The Journal of Rheumatology March 2010 ,37(3):491-49 DOI:<https://www.jrheum.org/content/37/3/491>
- Chandrashekara, Pampana S. Prevalence of vitamin D deficiency in children with lower respiratory tract infections. *Int J Contemp Pediatr*;2019 May,6(3):1041-1045Available from : <https://www.ijpediatrics.com/index.php/ijcp/article/download/2404/1642>
- Wayse, V., Yousafzai, A., Mogale, K. et al. Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 y. *Eur J Clin Nutr* 58, 563–567 (2004). Available from: <https://doi.org/10.1038/sj.ejcn.1601845>
- Alladi YR, Gopal J .vitamin D deficiency and relation to recurrent RTI in children less than 5 years. *IOSR – JDMS*; 2017 Aug, 16(8):88-96.Available from : <http://www.iosrjournals.org/iosr-jdms/papers/Vol16-issue8/Version-2/O1608028896.pdf>
- Sakamoto RR, Sunlight in vitamin D deficiency: clinical implications. *JNP*; 2019 February,15(4) :282-28. Available from: [https://www.npjjournal.org/article/S1555-4155\(18\)30749-9/pdf](https://www.npjjournal.org/article/S1555-4155(18)30749-9/pdf)
- Kulkarni SP, Ashok A, Chougule. Correlation of serum vitamin D levels and anemia in childhood pneumonia: a case control study from a rural area. *Int J Contemp Pediatr*; 2017 May, 4(3):2349-3291. Available from :<https://www.ijpediatrics.com/index.php/ijcp/article/view/746>
- Center for disease control and prevention. Vitamin D [internet].2021 [last reviewed- July 2, 2021].Availablefrom:<https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/diet-and-micronutrients/vitamin-d.html>
- Chowdhury R ,Taneja S, Sinha B et al. vitamin D deficiency predicts infections in young north Indian children: A secondary data analysis. *PLoS One*; 2017

- Mar, 12(3). Available from: <https://www.ncbi.nlm.nih.gov/pubmed/28273084>
22. Taylor SN. Vitamin D in Toddlers, Preschool Children, and Adolescents. *Ann Nutr Metab.* 2020;76 Suppl 2:30-41. doi: 10.1159/000505635. Epub 2020 Nov 24. PMID: 33232959.
DOI: <https://doi.org/10.1159/000505635>
 23. Nair H, Simões EA, Rudan I, et al. Global and regional burden of hospital admissions for severe acute lower respiratory infections in young children in 2010: a systematic analysis. *Lancet.* 2013;381(9875):1380-1390. doi:10.1016/S0140-6736(12)61901-1
 24. Laaksi Illka et al, *The Journal of Infectious Diseases*, Volume 202, Issue 5, 1 September 2010, Pages 809–814, <https://doi.org/10.1086/654881>
 25. Camargo CA et al, *Pediatrics* (2012) 130 (3): e561–e567